

NMCP COVID-19 Literature Report #39: Friday, 11 September 2020

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Purpose: These now weekly reports, published on Fridays, are curated collections of current research, evidence reviews, and news regarding the COVID-19 pandemic. Please feel free to reach out with questions, suggestions for future topics, or any other concerns.

All reports are available online at <https://nmcp.libguides.com/covidreport>. Access is private; you will need to use the direct link or bookmark the URL, along with the case-sensitive password "NMCPfinest".

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, things are changing rapidly, with new research and potentially conflicting literature published daily.

Statistics

Global today: 28,212,036 confirmed cases and 910,314 deaths in 188 countries/regions

last week: 26,347,573 confirmed cases and 869,600 deaths in 188 countries/regions

United States*

top 5 states by cases (Virginia is ranked 15th)

	TOTAL US	CA	TX	FL	NY	GA
Confirmed Cases	6,399,978	751,615	669,652	654,731	441,911	289,123
Tests	85,181,078	12,389,991	5,405,257	4,850,259	9,052,978	2,542,594
Deaths	191,811	14,000	13,930	12,326	75,584	6,894

*see census.gov for current US Population data; NA: not all data available

[JHU CSSE](https://www.jhu-csse.org) as of 1100 EDT 11 September 2020

<i>Virginia</i>	Total	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	131,640	4,026	1,690	2,532	4,612	2,343	1,780	6,368
Hospitalized	10,155	357	57	90	327	249	117	336
Deaths	2,711	49	16	28	61	45	63	71

[VA DOH](https://www.vahhs.org) as of 1100 EDT 11 September 2020

Special Reports and Other Items of Interest

NORC: [COVID Response Tracking Study](#)

This is an ongoing nationally representative, longitudinal study to understand Americans' beliefs, mental health, and outlook before, during and after the coronavirus outbreak. They have published the 'third wave' of results:

"[Findings from the third wave \[pdf\]](#) of 2020 data indicate that although the public's well-being took a historic hit earlier in the pandemic, over the course of the summer mental health has neither deteriorated further nor improved. The latest data also illuminate large health disparities in Americans' rates of experiencing 15 different psychosomatic symptoms associated with stress and anxiety. Younger adults, women, those with lower income or lower educational attainment, and those who often watch, read, or talk about the coronavirus report higher rates of various symptoms, compared to other groups."

Previously:

- [results from first wave \[pdf\]](#);
- [results from the first survey \[pdf\]](#);
- [results from the second wave \[pdf\]](#).

RF: [A National Decision Point: Effective Testing and Screening for Covid-19](#) (published 09 September 2020)

"Economic activity has plunged and a record number of Americans are out of work. Millions of jobs may have disappeared forever. Most of the nation's school children have not returned to classrooms full time this fall, straining families as well as employers.

This must change. The best tools for shifting back to some form of normalcy are effective masking and distancing measures to mitigate spread, coupled with sufficient Covid-19 tests paired with sophisticated strategies for their effective use. This report describes how to offer the latter in ways that can be tailored to local circumstances and risk tolerances. The goal is to give schools, businesses, and other critical institutions a pathway toward operating safely even for higher-risk populations and with continuing community spread.

There are four basic elements to a testing strategy that can contain outbreaks, inform public health decisionmaking, and respond to local Covid-19 prevalence rates:

- Assessments of the risks of infection and death depending on local spread and population characteristics.
- Meaningful and measurable goals for acceptable infection reduction through screening and surveillance.
- Calculation of budgetary and administrative constraints.
- Adequate supplies of sufficiently reliable tests."

Selected Literature: Peer-Reviewed Journals

Date given is the date published or posted online; often these papers are ahead of print.

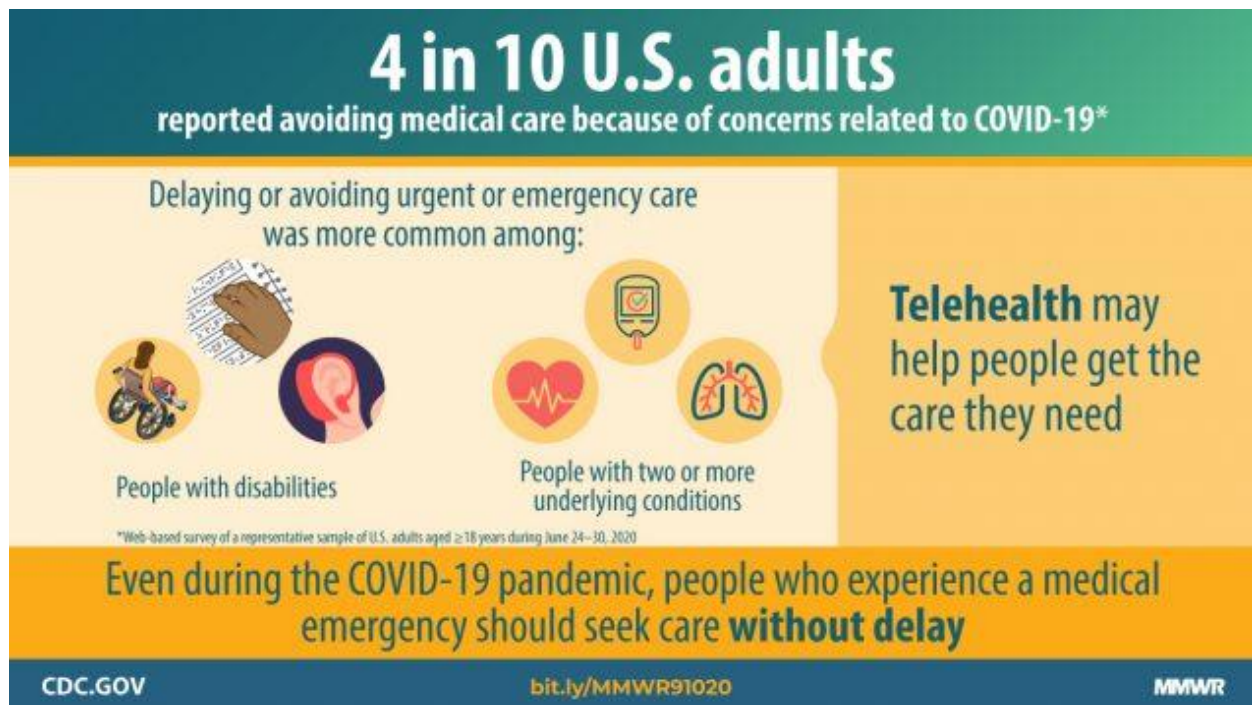
11 September 2020

MMWR: [Delay or Avoidance of Medical Care Because of COVID-19–Related Concerns — United States, June 2020](#)

"Delayed or avoided medical care might increase morbidity and mortality associated with both chronic and acute health conditions.

By June 30, 2020, because of concerns about COVID-19, an estimated 41% of U.S. adults had delayed or avoided medical care including urgent or emergency care (12%) and routine care (32%). Avoidance of urgent or emergency care was more prevalent among unpaid caregivers for adults, persons with underlying medical conditions, Black adults, Hispanic adults, young adults, and persons with disabilities.

Understanding factors associated with medical care avoidance can inform targeted care delivery approaches and communication efforts encouraging persons to safely seek timely routine, urgent, and emergency care."



MMWR: [Community and Close Contact Exposures Associated with COVID-19 Among Symptomatic Adults ≥18 Years in 11 Outpatient Health Care Facilities — United States, July 2020](#)

"Community and close contact exposures contribute to the spread of COVID-19.

Findings from a case-control investigation of symptomatic outpatients from 11 U.S. health care facilities found that close contact with persons with known COVID-19 or going to locations that offer on-site eating and drinking options were associated with COVID-19 positivity. Adults with positive SARS-CoV-2 test results were approximately twice as likely to have reported dining at a restaurant than were those with negative SARS-CoV-2 test results.

Eating and drinking on-site at locations that offer such options might be important risk factors associated with SARS-CoV-2 infection. Efforts to reduce possible exposures where mask use and social distancing are difficult to maintain, such as when eating and drinking, should be considered to protect customers, employees, and communities."

10 September 2020

JAMA: [Racial/Ethnic Variation in Nasal Gene Expression of Transmembrane Serine Protease 2 \(TMPRSS2\)](#)

"This study of nasal epithelial gene expression in a racially/ethnically diverse cohort showed significantly higher expression of TMPRSS2 in Black individuals compared with other self-identified races/ethnicities. Given the essential role of TMPRSS2 in SARS-CoV-2 entry,³ higher nasal expression of TMPRSS2 may contribute to the higher burden of COVID-19 among Black individuals. TMPRSS2 inhibitors such as camostat mesylate³ are undergoing clinical trials to test their utility for COVID-19 treatment. The finding of racial/ethnic variation in TMPRSS2 expression emphasizes that inclusion of diverse participants and analyses stratified by race/ethnicity should be incorporated into such trials."

JAMA Intern Med: [Effect of Recombinant Human Granulocyte Colony–Stimulating Factor for Patients With Coronavirus Disease 2019 \(COVID-19\) and Lymphopenia: A Randomized Clinical Trial](#)

"Question: Can treating patients with coronavirus disease 2019 (COVID-19) with recombinant human granulocyte colony-stimulating factor (rhG-CSF) increase their peripheral blood leukocyte and lymphocyte cell counts and lead to clinical improvement?

Findings: In this open-label, randomized clinical trial of 200 Chinese patients with COVID-19, lymphopenia, and no comorbidities, rhG-CSF treatment did not accelerate clinical improvement, but the number of patients progressing to critical illness or death may have been reduced, without an increased risk of serious adverse events.

Meaning: Preliminary findings from a randomized clinical trial suggest that rhG-CSF treatment should be studied in larger trials and a broader range of patients with COVID-19."

09 September 2020

BMJ: [Use of "normal" risk to improve understanding of dangers of covid-19](#)

"As covid-19 turns from a societal threat into a matter of risk management, it is vital that the associated risks are understood and clearly communicated. But these risks vary hugely between people, and so finding appropriate analogues is a challenge. Although covid-19 is a complex multisystem disease that can cause prolonged illness, here I focus solely on the risks of dying from covid-19 and explore the use of "normal" risk—the risk of death from all causes each year—as an aid to transparent communication."

Eur Resp J: [COVID-19 and Pneumothorax: A Multicentre Retrospective Case Series](#)

"Pneumothorax and pneumomediastinum have both been noted to complicate cases of COVID-19 requiring hospital admission. We report the largest case series yet described of patients with both these pathologies that includes non-ventilated patients.

Cases were collected retrospectively from UK hospitals with inclusion criteria limited to a diagnosis of COVID-19 and the presence of either pneumothorax or pneumomediastinum. Patients included in the study presented between March and June 2020. Details obtained from the medical record included demographics, radiology, laboratory investigations, clinical management and survival.

Seventy-one patients from 16 centres were included in the study, of whom 60 patients had pneumothoraces (six also with pneumomediastinum), whilst 11 patients had pneumomediastinum alone. Two of these patients had two distinct episodes of pneumothorax, occurring bilaterally in sequential fashion, bringing the total number of pneumothoraces included to 62. Clinical scenarios included patients who had presented to hospital with pneumothorax, patients who had developed pneumothorax or pneumomediastinum during their inpatient admission with COVID-19 and patients who developed their complication whilst intubated and ventilated, either with or without concurrent extracorporeal membrane oxygenation. Survival at 28 days was not significantly different following pneumothorax ($63.1\% \pm 6.5\%$) or isolated pneumomediastinum ($53.0\% \pm 18.7\%$; $p=0.854$). The incidence of pneumothorax was higher in males. The 28-day survival was not different between the sexes (males $62.5\% \pm 7.7\%$ versus females $68.4\% \pm 10.7\%$; $p=0.619$). Patients above the age of 70 had a significantly lower 28-day survival than younger individuals (≥ 70 years $41.7\% \pm 13.5\%$ survival versus < 70 years $70.9\% \pm 6.8\%$ survival; $p=0.018$ log-rank).

These cases suggest that pneumothorax is a complication of COVID-19. Pneumothorax does not seem to be an independent marker of poor prognosis and we encourage active treatment to be continued where clinically possible."

J Infect Dis: [Environmental and Aerosolized SARS-CoV-2 Among Hospitalized COVID-19 Patients](#)

"During April and May 2020, we studied 20 hospitalized COVID-19 patients, their hospital rooms (fomites and aerosols), and their close contacts for molecular and culture evidence of SARS-CoV-2 virus. Among the more than 400 samples, we found molecular evidence of virus in most sample types, especially the nasopharyngeal (NP), saliva, and fecal samples, but the prevalence of molecular positivity among fomites and aerosols was low. The agreement between NP swab and saliva positivity was high (89.5%, Kappa 0.79). Two NP swabs collected from patients on one and seven days post-symptom onset had evidence of infectious virus (2 passages over 14 days in Vero E6 cells). In summary, the low molecular prevalence and lack of viable SARS-CoV-2 virus in fomites and air samples implied low nosocomial risk SARS-CoV-2 transmission through inanimate objects or aerosols."

JAMA Intern Med: [Clinical Outcomes in Young US Adults Hospitalized With COVID-19](#)

"Young adults age 18 to 34 years hospitalized with COVID-19 experienced substantial rates of adverse outcomes: 21% required intensive care, 10% required mechanical ventilation, and 2.7% died. This in-hospital mortality rate is lower than that reported for older adults with COVID-19, but approximately double that of young adults with acute myocardial infarction. Morbid obesity, hypertension, and diabetes were common and associated with greater risks of adverse events. Young adults with more than 1 of these conditions faced risks comparable with those observed in middle-aged adults without them. More than half of these patients requiring hospitalization were Black or Hispanic, consistent with prior findings of disproportionate illness severity in these demographic groups."

JAMA Netw Open: [Incidence of Nosocomial COVID-19 in Patients Hospitalized at a Large US Academic Medical Center](#)

"Question: What is the incidence of hospital-acquired coronavirus disease 2019 (COVID-19) at a large US academic medical center?

Findings: In this cohort study of 9149 patients admitted to a large US academic medical center over a 12-week period, 697 were diagnosed with COVID-19. In the context of a comprehensive and progressive infection control program, only 2 hospital-acquired cases were detected: 1 patient was likely infected by a presymptomatic spouse before visitor restrictions were implemented, and 1 patient developed symptoms 4 days after a 16-day hospitalization but without known exposures in the hospital.

Meaning: These findings suggest that overall risk of hospital-acquired COVID-19 was low and that rigorous infection control measures may be associated with minimized risk."

Nat Commun: [Substantial underestimation of SARS-CoV-2 infection in the United States](#)

"Accurate estimates of the burden of SARS-CoV-2 infection are critical to informing pandemic response. Confirmed COVID-19 case counts in the U.S. do not capture the total burden of the pandemic because testing has been primarily restricted to individuals with moderate to severe symptoms due to limited test availability. Here, we use a semi-Bayesian probabilistic bias analysis to account for incomplete testing and imperfect diagnostic accuracy. We estimate 6,454,951 cumulative infections compared to 721,245 confirmed cases (1.9% vs. 0.2% of the population) in the United States as of April 18, 2020. Accounting for uncertainty, the number of infections during this period was 3 to 20 times higher than the number of confirmed cases. 86% (simulation interval: 64–99%) of this difference is due to incomplete testing, while 14% (0.3–36%) is due to imperfect test accuracy. The approach can readily be applied in future studies in other locations or at finer spatial scale to correct for biased testing and imperfect diagnostic accuracy to provide a more realistic assessment of COVID-19 burden."

08 September 2020

Cell: [Cancer, COVID-19, and antiviral immunity: the CAPTURE study](#)

"The SARS-CoV-2 pandemic has posed a significant challenge for risk evaluation and mitigation amongst cancer patients. Susceptibility to and severity of COVID-19 in cancer patients has not been studied in a prospective and broadly applicable manner. CAPTURE is a pan-cancer, longitudinal immune profiling study designed to address this knowledge gap."

JAMA Netw Open: [Comparison of Clinical Features of COVID-19 vs Seasonal Influenza A and B in US Children](#)

"Question: What are the similarities and differences in clinical features between coronavirus disease 2019 (COVID-19) and seasonal influenza in US children?

Findings: In this cohort study of 315 children with COVID-19 and 1402 children with seasonal influenza, there were no statistically significant differences in the rates of hospitalization, admission to the intensive care unit, and mechanical ventilator use between the 2 groups. More patients with COVID-19 than with seasonal influenza reported fever, diarrhea or vomiting, headache, body ache, or chest pain at the time of diagnosis.

Meaning: The findings suggest that prevention of both COVID-19 and seasonal influenza in US children is prudent and urgent for the well-being of this population."

PLoS Med: [Adverse outcomes and mortality in users of non-steroidal anti-inflammatory drugs who tested positive for SARS-CoV-2: A Danish nationwide cohort study](#)

"Author summary: During the early phases of the pandemic of coronavirus disease 2019 (COVID-19), concerns were raised that ibuprofen, a drug commonly used to treat weak pain and fevers, may lead to a more severe course of coronavirus disease.

If this risk is verified, it would be important to reduce the use of ibuprofen and ibuprofen-like drugs, commonly referred to as non-steroidal anti-inflammatory drugs (NSAIDs), among patients at risk of COVID-19.

We identified all Danish residents who tested positive for the infectious agent of COVID-19 and grouped them into users and non-users of NSAIDs.

The risks of being hospitalized, admitted to the intensive care unit, or dying were compared between the 2 groups.

Overall, risks for all studied outcomes were similar between users and non-users of ibuprofen and other NSAIDs.

NSAIDs do not lead to more severe coronavirus disease according to this study."

06 September 2020

Cell: [The Immunology of Multisystem Inflammatory Syndrome in Children with COVID-19](#)

Highlights:

- Hyperinflammation in MIS-C differs from that of acute COVID-19
- T-cell subsets discriminate Kawasaki disease patients from MIS-C
- IL-17A drives Kawasaki, but not MIS-C hyperinflammation
- Global profiling reveals candidate autoantibodies with pathogenic potential

Transbound Emerg Dis: [Decreased Case Fatality Rate of COVID-19 in the Second Wave: a study in 53 countries or regions](#)

"The raw case fatality rate (CFR, reported number of COVID-19 deaths divided by the number of cases) is an important indicator to quantify the severity or treatment efficacy. In many countries, the pandemic had two waves to date. To our knowledge, no studies have compared the CFR between the two waves. In this work, we report that of 53 countries or regions with the highest death tolls, 43 had lower CFR estimates in the on-going second wave than in the first wave. We discussed the possible reasons. Also, we compared the two-wave pattern of COVID-19 with those of influenza. Influenza activities in the pre-pandemic era provided an indicator for seasonality of climate in a country. The sharp drop in 2020 influenza activity is an indicator of the effects of social distancing."

04 September 2020

EClinicalMedicine: [Multisystem inflammatory syndrome in children: A systematic review](#)

"Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread throughout the world at an alarming rate. Previous reports suggested that children infected with coronavirus disease 2019 (COVID-19), the condition caused by SARS-CoV-2, were highly resilient and had mild symptoms. As of late April 2020, reports from the United Kingdom surfaced describing a new hyperinflammatory disease that is temporally associated with SARS-CoV-2 infection. Since then, several other countries have also reported patients exhibiting similar features, and this phenomenon has subsequently been coined multisystem inflammatory syndrome in children (MIS-C) or pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS). In this context, our goal was to provide a review of published articles focusing on MIS-C.

This systematic review summarizes the clinical presentation of MIS-C from 662 patients (n = 39 studies). We report the most common signs and symptoms, quantify laboratory findings, and describe imaging characteristics of children with MIS-C. Furthermore, we summate outcomes, treatments, and compare MIS-C to COVID-19.

Results from this systematic review represent a comprehensive evaluation of children meeting MIS-C criteria. Our findings will inform clinicians of the signs, markers, and outcomes of children who develop this dangerous and potentially life-threatening hyperinflammatory syndrome. Future research should focus on identifying variables that can prognosticate which pediatric COVID-19 patients will develop MIS-C and which, if any, markers correlate with systemic outcomes."

Lancet: [Azithromycin in addition to standard of care versus standard of care alone in the treatment of patients admitted to the hospital with severe COVID-19 in Brazil \(COALITION II\): a randomised clinical trial](#)

"To the best of our knowledge, this study is the first randomised clinical trial assessing the effect of azithromycin added to a standard of care regimen that includes hydroxychloroquine, on a patient-centred outcome in patients with severe COVID-19. We provided detailed and clear descriptions of clinical parameters, and clinical outcomes. In patients admitted to hospital with severe COVID-19, addition of azithromycin to a standard of care that included hydroxychloroquine did not result in clinical improvement or mortality reduction. Furthermore, contrary to what has been shown in observational studies, adding azithromycin to hydroxychloroquine did not result in higher rates of reported prolongation of QTc interval, cardiac arrest, or ventricular arrhythmias.

Because azithromycin is among the most widely prescribed drugs worldwide to treat COVID-19, our results showing that it did not improve outcomes compared with standard of

care will inform physicians and might affect clinical practice and future research in this field."

Pediatr Blood Cancer: [Convalescent plasma for pediatric patients with SARS-CoV-2-associated acute respiratory distress syndrome](#)

"There are no proven safe and effective therapies for children who develop life-threatening complications of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Convalescent plasma (CP) has demonstrated potential benefit in adults with SARS-CoV-2, but has theoretical risks. We present the first report of CP in children with life-threatening coronavirus disease 2019 (COVID-19), providing data on four pediatric patients with acute respiratory distress syndrome. We measured donor antibody levels and recipient antibody response prior to and following CP infusion. Infusion of CP was not associated with antibody-dependent enhancement (ADE) and did not suppress endogenous antibody response. We found CP was safe and possibly efficacious. Randomized pediatric trials are needed."

03 September 2020

Eur Heart J: [COVID-19 is, in the end, an endothelial disease](#)

"The vascular endothelium provides the crucial interface between the blood compartment and tissues, and displays a series of remarkable properties that normally maintain homeostasis. This tightly regulated palette of functions includes control of haemostasis, fibrinolysis, vasomotion, inflammation, oxidative stress, vascular permeability, and structure. While these functions participate in the moment-to-moment regulation of the circulation and coordinate many host defence mechanisms, they can also contribute to disease when their usually homeostatic and defensive functions over-reach and turn against the host. SARS-CoV-2, the aetiological agent of COVID-19, causes the current pandemic. It produces protean manifestations ranging from head to toe, wreaking seemingly indiscriminate havoc on multiple organ systems including the lungs, heart, brain, kidney, and vasculature. This essay explores the hypothesis that COVID-19, particularly in the later complicated stages, represents an endothelial disease. Cytokines, protein pro-inflammatory mediators, serve as key danger signals that shift endothelial functions from the homeostatic into the defensive mode. The endgame of COVID-19 usually involves a cytokine storm, a phlogistic phenomenon fed by well-understood positive feedback loops that govern cytokine production and overwhelm counter-regulatory mechanisms. The concept of COVID-19 as an endothelial disease provides a unifying pathophysiological picture of this raging infection, and also provides a framework for a rational treatment strategy at a time when we possess an indeed modest evidence base to guide our therapeutic attempts to confront this novel pandemic."

JAMA: [Cytokine Levels in Critically Ill Patients With COVID-19 and Other Conditions](#)

"In this study, critically ill patients with COVID-19 with ARDS had circulating cytokine levels that were lower compared with patients with bacterial sepsis and similar to other critically ill patients. These findings are in line with lower leukocyte counts observed in patients with COVID-19, and are possibly due to lower overall disease severity, despite the presence of severe pulmonary injury. The findings of this preliminary analysis suggest COVID-19 may not be characterized by cytokine storm. Whether anticytokine therapies will benefit patients with COVID-19 remains to be determined."

JAMA Netw Open: [Association of Vitamin D Status and Other Clinical Characteristics With COVID-19 Test Results](#)

"Findings: In this cohort study of 489 patients who had a vitamin D level measured in the year before COVID-19 testing, the relative risk of testing positive for COVID-19 was 1.77 times greater for patients with likely deficient vitamin D status compared with patients with likely sufficient vitamin D status, a difference that was statistically significant.

Meaning: These findings appear to support a role of vitamin D status in COVID-19 risk; randomized clinical trials are needed to determine whether broad population interventions and interventions among groups at increased risk of vitamin D deficiency and COVID-19 could reduce COVID-19 incidence."

JASN: [AKI in Hospitalized Patients with COVID-19](#)

"Early reports have indicated that AKI and other kidney abnormalities are associated with coronavirus disease 2019 (COVID-19). Of 3993 hospitalized patients with COVID-19 in a New York City health system, AKI occurred in 1835 (46%) patients; among patients with AKI, 19% required dialysis, and half of them died in the hospital. Among patients who were discharged, 35% had not recovered to baseline kidney function at the time of discharge. AKI is common among patients with COVID-19 and is associated with higher mortality than in patients without AKI; among those who survive, only about a third are discharged with renal recovery. These findings may help centers with resource planning and preparing for the increased load resulting from survivors of COVID-19—associated AKI who do not experience recovery of kidney function."

ICYMI

AJRCCM: [Pulmonary Vascular Dilatation Detected by Automated Transcranial Doppler in COVID-19 Pneumonia](#) (posted 06 August 2020)

Letter to the editor that may explain how some patients with severe hypoxemia had well preserved lung compliance.

Cell: [Effects of COVID-19 on the Nervous System](#) (posted 19 August 2020)

"Neurological complications have emerged as a significant cause of morbidity and mortality in the ongoing COVID-19 pandemic. Beside respiratory insufficiency, many hospitalized patients exhibit neurological manifestations ranging from headache and loss of smell, to confusion and disabling strokes. COVID-19 is also anticipated to take a toll on the nervous system in the long term. Here, we will provide a critical appraisal of the potential for neurotropism and mechanisms of neuropathogenesis of SARS-CoV-2 as they relate to the acute and chronic neurological consequences of the infection. Finally, we will examine potential avenues for future research and therapeutic development."

Clin Infect Dis: [Empiric Antibacterial Therapy and Community-onset Bacterial Co-infection in Patients Hospitalized with COVID-19: A Multi-Hospital Cohort Study](#) (posted 21 August 2020)

"Randomly sampled cohort of 1705 patients hospitalized with COVID-19 in 38 Michigan hospitals between 3/13/2020-6/18/2020. Data were collected on early (prescribed within 2 days of hospitalization) empiric antibacterial therapy and community-onset bacterial co-infections (positive culture or diagnostic test within 3 days). Poisson generalized estimating equation models were used to assess predictors of empiric antibacterial use.

Of 1705 patients with COVID-19, 56.6% were prescribed early empiric antibacterial therapy; 3.5% (59/1705) had a confirmed community-onset bacterial infection. Across hospitals, early empiric antibacterial use varied from 27%-84%. Patients were more likely to receive early empiric antibacterial therapy if they were older (adjusted rate ratio [ARR]: 1.04 [1.00-1.08] per 10 years), had a lower body mass index (ARR: 0.99 [0.99-1.00] per kg/m²), had more severe illness (e.g., severe sepsis, ARR: 1.16 [1.07-1.27]), had a lobar infiltrate (ARR: 1.21 [1.04-1.42]), or were admitted to a for-profit hospital (ARR: 1.30 [1.15-1.47]). Over time, COVID-19 test turnaround time (returned ≤ 1 day in March [54.2%, 461/850] vs. in April [85.2%, 628/737], $P < .001$) and empiric antibacterial use (ARR: 0.71 [0.63-0.81] April vs. March) decreased.

The prevalence of confirmed community-onset bacterial co-infections was low. Despite this, half of patients received early empiric antibacterial therapy. Antibacterial use varied widely by hospital. Reducing COVID-19 test turnaround time and supporting stewardship could improve antibacterial use."

Obes Rev: [Individuals with obesity and COVID-19: A global perspective on the epidemiology and biological relationships](#) (posted 26 August 2020)

"The linkage of individuals with obesity and COVID-19 is controversial and lacks systematic reviews. After a systematic search of the Chinese and English language literature on COVID-19, 75 studies were used to conduct a series of meta-analyses on the relationship of individuals with obesity–COVID-19 over the full spectrum from risk to mortality. A systematic review of the mechanistic pathways for COVID-19 and individuals with obesity is

presented. Pooled analysis show individuals with obesity were more at risk for COVID-19 positive, >46.0% higher (OR = 1.46; 95% CI, 1.30–1.65; $p < 0.0001$); for hospitalization, 113% higher (OR = 2.13; 95% CI, 1.74–2.60; $p < 0.0001$); for ICU admission, 74% higher (OR = 1.74; 95% CI, 1.46–2.08); and for mortality, 48% increase in deaths (OR = 1.48; 95% CI, 1.22–1.80; $p < 0.001$). Mechanistic pathways for individuals with obesity are presented in depth for factors linked with COVID-19 risk, severity and their potential for diminished therapeutic and prophylactic treatments among these individuals. Individuals with obesity are linked with large significant increases in morbidity and mortality from COVID-19. There are many mechanisms that jointly explain this impact. A major concern is that vaccines will be less effective for the individuals with obesity."

Selected Literature: Preprints

Preprints are found on preprint servers such as [arXiv](#), [bioRxiv](#), and [medRxiv](#); they are commonly used for biomedical research.

Per medRxiv: "Preprints are preliminary reports of work that have not been certified by peer review. They should not be relied on to guide clinical practice or health-related behavior and should not be reported in news media as established information."

Preprints may later be published in peer-reviewed journals.

medRxiv: [Gastrointestinal involvement attenuates COVID-19 severity and mortality](#) (posted 09 September 2020)

"Given that gastrointestinal (GI) symptoms are a prominent extrapulmonary manifestation of coronavirus disease 2019 (COVID-19), we investigated the impact of GI infection on disease pathogenesis in three large cohorts of patients in the United States and Europe. Unexpectedly, we observed that GI involvement was associated with a significant reduction in disease severity and mortality, with an accompanying reduction in key inflammatory proteins including IL-6, CXCL8, IL-17A and CCL28 in circulation. In a fourth cohort of COVID-19 patients in which GI biopsies were obtained, we identified severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) within small intestinal enterocytes for the first time in vivo but failed to obtain culturable virus. High dimensional analyses of GI tissues confirmed low levels of cellular inflammation in the GI lamina propria and an active downregulation of key inflammatory genes including IFNG, CXCL8, CXCL2 and IL1B among others. These data draw attention to organ-level heterogeneity in disease pathogenesis and highlight the role of the GI tract in attenuating SARS-CoV-2-associated inflammation with related mortality benefit."

bioRxiv: [Neuroinvasion of SARS-CoV-2 in human and mouse brain](#) (posted 09 September 2020)

"Although COVID-19 is considered to be primarily a respiratory disease, SARS-CoV-2 affects multiple organ systems including the central nervous system (CNS). Yet, there is no consensus whether the virus can infect the brain, or what the consequences of CNS infection are. Here, we used three independent approaches to probe the capacity of SARS-CoV-2 to infect the brain. First, using human brain organoids, we observed clear evidence of infection with accompanying metabolic changes in the infected and neighboring neurons. However, no evidence for the type I interferon responses was detected. We demonstrate that neuronal infection can be prevented either by blocking ACE2 with antibodies or by administering cerebrospinal fluid from a COVID-19 patient. Second, using mice overexpressing human ACE2, we demonstrate in vivo that SARS-CoV-2 neuroinvasion, but not respiratory infection, is associated with mortality. Finally, in brain autopsy from patients who died of COVID-19, we detect SARS-CoV-2 in the cortical neurons, and note pathologic features associated with infection with minimal immune cell infiltrates. These results provide evidence for the neuroinvasive capacity of SARS-CoV2, and an unexpected consequence of direct infection of neurons by SARS-CoV-2."

medRxiv: [The timing of COVID-19 transmission](#) (posted 07 September 2020)

"The timing of SARS-CoV-2 transmission is a critical factor to understand the epidemic trajectory and the impact of isolation, contact tracing and other non-pharmaceutical interventions on the spread of COVID-19 epidemics. We examined the distribution of transmission events with respect to exposure and onset of symptoms. We show that for symptomatic individuals, the timing of transmission of SARS-CoV-2 is more strongly linked to the onset of clinical symptoms of COVID-19 than to the time since infection. We found that it was approximately centered and symmetric around the onset of symptoms, with three quarters of events occurring in the window from 2-3 days before to 2-3 days after. However, we caution against overinterpretation of the right tail of the distribution, due to its dependence on behavioural factors and interventions. We also found that the pre-symptomatic infectious period extended further back in time for individuals with longer incubation periods. This strongly suggests that information about when a case was infected should be collected where possible, in order to assess how far into the past their contacts should be traced. Overall, the fraction of transmission from strictly pre-symptomatic infections was high (41%; 95%CI 31-50%), which limits the efficacy of symptom-based interventions, and the large fraction of transmissions (35%; 95%CI 26-45%) that occur on the same day or the day after onset of symptoms underlines the critical importance of individuals distancing themselves from others as soon as they notice any symptoms, even if they are mild. Rapid or at-home testing and contextual risk information would greatly facilitate efficient early isolation."

medRxiv: [A neutrophil activation signature predicts critical illness and mortality in COVID-19](#)
(posted 02 September 2020)

"Pathologic immune hyperactivation is emerging as a key feature of critical illness in COVID-19, but the mechanisms involved remain poorly understood. We carried out proteomic profiling of plasma from cross-sectional and longitudinal cohorts of hospitalized patients with COVID-19 and analyzed clinical data from our health system database of over 3,300 patients. Using a machine learning algorithm, we identified a prominent signature of neutrophil activation, including resistin, lipocalin-2, HGF, IL-8, and G-CSF, as the strongest predictors of critical illness. Neutrophil activation was present on the first day of hospitalization in patients who would only later require transfer to the intensive care unit, thus preceding the onset of critical illness and predicting increased mortality. In the health system database, early elevations in developing and mature neutrophil counts also predicted higher mortality rates. Altogether, we define an essential role for neutrophil activation in the pathogenesis of severe COVID-19 and identify molecular neutrophil markers that distinguish patients at risk of future clinical decompensation."

Upcoming Events (Webinars, Calls, etc.)

WHAT: CDC COCA: Telehealth & Health Equity: Considerations for Addressing Health Disparities during the COVID-19 Pandemic

WHEN: Tuesday, 15 SEP 2020 1400-1500 EDT

OVERVIEW: During this COCA Call, presenters will discuss the intersection of telehealth and health equity and implications for health services during the COVID-19 pandemic. Presenters will identify long-standing systemic health and social inequities that contribute to COVID-19 health disparities, while highlighting opportunities and limitations of telehealth implementation as an actionable solution.

Includes continuing education (CE) credit.

DETAILS: https://emergency.cdc.gov/coca/calls/2020/callinfo_091520.asp

WHAT: CDC COCA: Testing and Treatment of 2020-2021 Seasonal Influenza During the COVID-19 Pandemic

WHEN: Thursday, 17 SEP 2020 1400-1500 EDT

OVERVIEW: During this COCA call, clinicians will hear an overview of CDC's recommendations for health care providers regarding influenza diagnostics and the use of antiviral

medications for the 2020-2021 influenza season, including considerations during the ongoing COVID-19 pandemic.

Includes continuing education (CE) credit.

DETAILS: https://emergency.cdc.gov/coca/calls/2020/callinfo_091720.asp

WHAT: [Hidden Consequences: How the COVID Pandemic is Impacting Children Series-Child Health and Wellness Webinar](#)

WHEN: Wednesday, 30 SEP 2020 1330-1445 EDT

DETAILS: Assistant Secretary for Preparedness and Response (ASPR), Technical Resources, Assistance Center, and Information Exchange (TRACIE) and ASPR's Pediatric Centers of Excellence are collaborating on a webinar series focused on the impact of the COVID-19 pandemic on children. Topics will include impact on child health and wellness, child emotional and social impact, and impact of COVID-19 on children with special healthcare needs, and how secondary/other disasters affect children during the pandemic.

The first webinar in this series will focus on child health and wellness. Panelists will discuss resumption of routine care, missed immunizations and lead poisoning screening, sleep, and child neglect and abuse.

REGISTER: <https://register.gotowebinar.com/register/403704795003207440>

News in Brief

According to a new poll, about half of active-duty service members believe the ongoing coronavirus pandemic represents a significant threat to military readiness and operations ([Military Times](#)).

Long read: "The pandemic is an intuition nightmare: As the US heads towards the winter, the country is going round in circles, making the same conceptual errors that have plagued it since spring." ([Atlantic](#))

Transmission and Mutations

It is highly unlikely that food is a source of coronavirus transmission, according to an international team of experts ([CNN](#); [full report from ICMSF \[pdf\]](#)).

If you are hanging your hat on herd immunity, the cost may be more than a million deaths ([Medpage](#)).

Long read: "The coronavirus is mutating — does it matter?" ([Nature](#))

Testing and Treatments

A British start-up company, iAbra, says it has developed a 20-second saliva COVID-19 test with a sensitivity of 99.8% and specificity of 96.7% ([Reuters](#)).

South Korea company Celltrion will start production of an experimental antibody drug for COVID-19 ([Reuters](#)).

Senegal, a country with about 7 doctors for every 100,000 people, is a COVID-19 success story ([USA Today](#)).

Vaccines

AstraZeneca's phase 3 COVID-19 vaccine trial (aka the Oxford study) is on hold due to a suspected adverse reaction in a volunteer ([STAT](#)).

Nine drug companies — AstraZeneca, Moderna, Pfizer, Johnson & Johnson, GlaxoSmithKline, Merck, Novavax, BioNTech, and Sanofi — signed a pledge to abide by "high ethical standards and sound scientific principles" in developing a COVID-19 vaccine; as part of the pledge, the companies will not submit for FDA approval until the safety and efficacy of a vaccine has been shown in large clinical trials ([NPR](#)).

In an open letter to the editor at The Lancet, 26 experts question the data on Russia's Sputnik-V COVID-19 vaccine, saying there are patterns in the data that are "highly unlikely" ([Reuters](#)).

OWS is an ambitious scientific endeavor; here's an assessment on where things stand ([STAT](#)).

Even if we get a coronavirus vaccine, most people won't be allowed to get it as soon as it's approved ([WaPo](#)).

October 22 is potentially a critical date for any coronavirus vaccine — that's when the FDA's vaccines advisory committee is next expected to meet; the meeting will be available to watch online ([FDA](#)).

Don't forget about the 'underdog' coronavirus vaccines we might need as backup plan ([Nature](#)).

Risk Factors and Ripple Effects

According to a new report on a worst case scenario superspreader event, the Sturgis Motorcycle Rally — a 460,000 person event held last month in South Dakota — could link 266,000 COVID-19 cases and have a public health price tag of \$12.2 billion ([WaPo](#); [full report](#)).

Post-intensive care syndrome (PICS) is a problem for COVID-19 patients ([Medpage](#)).

The pandemic is making eating disorders /disordered eating tendencies worse ([NPR](#)).

Multidisciplinary recovery programs are addressing the needs of COVID long-haulers ([Medpage](#)).

Long read: "Italy's Bergamo is calling back coronavirus survivors. About half say they haven't fully recovered." ([WaPo](#))

Focus on HCWs

The FDA has an app to help frontline providers; the app, [Cure ID](#), is part of an online repository for reporting and discovering treatment options for COVID-19 ([CNN](#); [FDA](#))

A survey of doctors in the UK's NHS found that two-thirds want to quit or plan to leave within 3 years, citing burnout and frustration over pay and handling of the pandemic ([Guardian](#)).

Long read: "A doctor went to his own employer for a COVID-19 antibody test. It cost \$10,984." ([ProPublica](#))

Back to School (or Home)

"Half a million US children have been diagnosed with Covid-19, according to the American Academy of Pediatrics and the Children's Hospital Association" ([CNN](#)).

At least 3 teachers in 3 states have died from coronavirus since the start of the new school year ([AP](#)).

Schools are struggling to feed children who rely on free or reduced-price meals ([NPR](#)).

College towns are the new front in the pandemic as students return and coronavirus cases spike with them ([NYT](#)).

More than 51,000 cases of coronavirus are reported at colleges and universities around the country ([NYT](#)). Virginia had 1,174 cases at 33 schools, including 31 at EVMS in Norfolk, according the NYT tracker, which was last updated on 03 September 2020 as of this writing.

Other Infectious Diseases and Outbreaks

The 11th Ebola outbreak in the DRC is now at 113 cases and 48 deaths ([WHOAFRO](#)).

Long read: "The 1918 flu is still with us': The deadliest pandemic ever is still causing problems today" ([WaPo](#)).

Thanks, Coronavirus

The financial burden of the pandemic – from job loss to reduction of wages or work hours – is bad, but a new survey of residents in New York City, Los Angeles, Chicago, and Houston shows it's even worse than expected ([NPR](#)).

"The share of 18- to 29-year-olds living with their parents has become a majority since US coronavirus cases began spreading early this year, surpassing the previous peak during the Great Depression era." ([Pew](#))

Child care centers are yet another victim of the pandemic ([NPR](#)).

Post-Pandemic Digital Magazine

"The Carnegie Endowment for International Peace ([CEIP](#)) convened 150 scholars from 20 nations to create a digital magazine that provides 'grounded, fresh analysis and new approaches to some of the most consequential challenges unfolding before us.' The magazine, "[The Day After: Navigating a Post-Pandemic World](#)," covers a range of important topics like nuclear arms control, disinformation, climate change, and the foreign and domestic policies of several countries. Current featured essays include 'India's Path to the Big Leagues' by Ashley J Tellis, 'Securing Cyberspace' by Michael Nelson and George Perkovich, and 'A Coming Decade of Arab Decisions' by Marwan Muasher and Maha Yahya." ([Pandora Report](#))

Odds and Ends

Remember those instant hospitals built in Wuhan early in the pandemic? If you are curious to know what happened to them, this report answers that question ([NPR](#)).

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Special Reports and Other Publications

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